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Research

Evaluation of Nosocomial Infections in a Tertiary Pediatric Intensive Care Unit

Üçüncü Basamak Bir Pediatrik Yoğun Bakım Ünitesinde Nozokomiyal Enfeksiyonların Değerlendirilmesi

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ABSTRACT

Objective: Nosocomial infections are an important preventable cause of increased morbidity and mortality in critically ill children. Our study compared the clinical features, laboratory data, and prognostic variables of nosocomial infections (NI) in children in the tertiary pediatric intensive care unit (PICU).

Methods: A retrospective evaluation of 48 pediatric patients aged 1 month to 18 years who had been admitted between February 2022 and January 2023 at University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital was performed. Children with NI were included. Demographic clinical and outcome data were analyzed.

Results: Twenty-seven patients (56.3%) were males. The median age was 32 months, and the length of stay in the PICU was 25 days (7-114). Respiratory diseases (50%) were the most common reasons for admission to the PICU, followed by sepsis (22.9%) and trauma (12.5%). The mortality rate was 18.8%. The requirement for renal replasman treatment was significantly higher in the non-survival group (p=0.017). Patients had similar prolonged PICU stay rates and requirements of mechanical ventilation, plasma exchange, and inotropic agents (p=0.472, p=0.320, p=0.432, p=0.068). Procalcitonin (PCT) (p=0.015), and procalcitonin/albumin ratio (PAR) (p=0.016) were also higher in the non-survival group than those in the survival group. Receiver operating characteristic (ROC) curves were used to predict mortality with PCT and PAR. According to ROC analysis, the cut-off values for PCT and PAR were found to be 1.705 (p=0.015), and 0.538 (p=0.016) respectively.

Conclusion: Risk factors that cannot be changed, such as the underlying disease, should be considered in patients. Other modifiable risk factors for NIs will likely be the focus of efforts to enhance patient care.

Keywords: Culture, nosocomial infection, organ dysfunction, pediatrics, sepsis

ÖZ

Amaç: Nozokomiyal enfeksiyonlar (NE), kritik hasta çocuklarda artmış morbidite ve mortalitenin önlenebilir önemli bir nedenidir. Çalışmamız, üçüncü basamak çocuk yoğun bakım ünitesindeki (ÇYBÜ) çocuklarda NE'lerin klinik özelliklerini, laboratuvar verilerini ve prognostik değişkenlerini karşılaştırdı.

Gereç ve Yöntem: Şubat 2022 ve Ocak 2023 tarihleri arasında Sağlık Bilimleri Üniversitesi, Sancaktepe Şehit Prof. Dr. İlhan Varank Eğitim ve Araştırma Hastanesi'ne başvuran 1 ay-18 yaş arası 48 çocuk hastanın retrospektif değerlendirmesi yapıldı. NE olan çocuklar dahil edildi. Demografik veriler, klinik değişkenler ve sonuç verileri analiz edildi.

Bulgular: Yirmi yedi hasta (%56,3) erkekti. Ortanca yaş 32 aydı ve ÇYBÜ'de kalış süresi 25 gündü (7-114). En sık başvuru nedeni solunum yolu hastalıkları (%50) olurken, bunu sepsis (%22,9) ve travma (%12,5) takip etti. Mortalite oranı %18,8 idi. Renal replasman tedavisi gereksinimi sağ kalamayan grupta anlamlı olarak daha yüksekti (p=0,017). Hastaların benzer uzamış ÇYBÜ kalış oranları ve mekanik ventilasyon, plazma değişimi ve inotropik ajan gereksinimleri vardı (p=0,472, p=0,320, p=0,432, p=0,068). Prokalsitonin (PCT) (p=0,015) ve prokalsitonin/albumin oranı (PAR)

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(p=0,016) da yaşamayan grupta yaşayan gruba göre daha yüksekti. PCT ve PAR ile mortaliteyi tahmin etmek için alıcı işletim karakteristik (ROC) eğrileri kullanıldı. ROC analizine göre PCT ve PAR için cut-off değerleri sırasıyla 1,705 (p=0,015) ve 0,538 (p=0,016) olarak bulundu.

Sonuç: Hastalarda altta yatan hastalık gibi değiştirilemeyen risk faktörleri göz önünde bulundurulmalıdır. NE'ler için diğer değiştirilebilir risk faktörleri, muhtemelen hasta bakımını iyileştirme çabalarının odak noktası olacaktır.

Anahtar Kelimeler: Kültür, nozokomiyal enfeksiyon, organ disfonksiyonu, pediatri, sepsis

INTRODUCTION

Nosocomial infection (NI) is a prevalent global health problem, particularly in pediatric intensive care units (PICU), and is associated with high mortality and morbidity, prolonged hospital stays, and high costs (1,2). There are numerous risk factors for NIs in critically ill children. In PICUs, there is frequent utilization of invasive medical devices, including endotracheal tubes (ETTs), central venous catheters (CVCs), and urine catheters. It is well-recognized that these devices increase the risk of NI (3).

The risk of nosocomial sepsis among critically ill children hospitalized in the PICU for more than two weeks is 50%. Although prevention bundles can reduce NI rates, this risk cannot be eliminated (4). Patients with NIs were found to have higher rates of poor outcomes and organ dysfunction. The overall mortality rate of NIs in children is estimated to be 11% (5). However, different factors, such as the presence of multiresistant microorganisms, affect prognosis, as shown in the literature (6).

Our study compared the clinical and demographic characteristics, laboratory parameters, and prognostic factors of NIs in children hospitalized in tertiary PICUs.

METHODS

This retrospective study was conducted in the PICU at Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital, University of Health Sciences Türkiye. Healthcare provision for children aged from 1 month to 18 years is provided in our PICU, which is equipped with 12 beds, 12 ventilators, 5 Prismaflex™ hemofiltration machines (Baxter, USA), and 9 isolation rooms.

A retrospective evaluation of 48 pediatric patients aged 1 month to 18 years who had been admitted between February 2022 and January 2023, if they met the criteria for NI, was included in the study. Patients who did not meet these criteria were excluded from the study. In our 12-bed PICU, 456 patients were hospitalized and followed up during the study period.

The Center for Disease Control criteria were used for the diagnosis of NI. An infection was defined as nosocomial when it occurred 48 hours (h) after admission to the PICU, and there was no evidence that the infection was present or incubated at the time of admission to the PICU. Children were evaluated for catheter-related bloodstream infection (CRBSI), ventilator-associated pneumonia (VAP), and catheter-associated urinary tract infections (CAUTI) (7).

CRBSI was defined as 2 positive blood cultures and the presence of one of the following symptoms in the case of a positive blood culture for a known pathogen unrelated to an infection at another site or commensal organisms: fever (>38 °C), chills at the insertion site, hypotension, or the appearance of infection. To be included in this study, the patient had to have a CVC within 48 h before this event (5).

We obtained informed consent from all parents before hospitalization and during all procedures. University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-invasive Research Ethics Committee approval was obtained from the hospital (decision no: 29, date: 15.02.2023). This study was conducted in accordance with the ethical rules of the Declaration of Helsinki Principles.

A detailed form was used for data collection regarding the patient's age, gender, length of stay in the PICU, duration of invasive mechanical ventilation (IMV), extracorporeal treatment requirement, inotropic treatment, laboratory parameters on the day of NI detection, treatment outcomes, and mortality. The blood sampling data of all cases were measured at almost the same time from the onset, and the worst value in the first 24 h of admission was recorded. Complete blood count, serum albumin, lactate dehydrogenase; procalcitonin (PCT), C-reactive protein (CRP) levels, and blood gas analysis on admission were retrospectively recorded from our electronic health information system. For the calculation of the Pediatric Risk of Mortality III (PRISM III) score, data from 16 variables regarding temperature, systolic blood pressure, heart rate, partial pressure of arterial oxygen, partial pressure of arterial carbon dioxide, Glasgow coma score, pupillary reaction, prothrombin time and activated partial thromboplastin time, serum creatinine, serum urea nitrogen, serum potassium, blood glucose, and serum bicarbonate levels, white blood cell and platelet counts were recorded within 24 h of PICU admission (8).

To detect pathogens in patients, double blood cultures were obtained from two sites at admission, and other biological samples were also collected for culture, including sputum, pleural effusion, ascites, urine, feces, pus, and others, according to the suspected infection site. Double blood cultures, including those of the CVC and peripheral vein, were taken in patients with suspected catheter infection. The volume of blood collected was determined according to the weight of the patient (9).

For the diagnosis of VAP, tracheobronchial samples were collected via deep tracheal aspirates from ETTs using a closed aspiration technique, and urine samples were aseptically aspirated from the urinary catheter sampling port. The number of colony-forming units (CFU/mL) in urine culture was considered to be more than 10^5 CFU/mL (7).

Statistical Analysis

SPSS statistical software 20.0 for Windows was used for statistical analyzes numbers, frequencies (%), ratios, medians, and standard deviation values were used in the descriptive statistics of the data. The distribution of variables was checked using the Kolmogorov-Smirnov test. During the analysis of quantitative data, t-tests and Mann-Whitney U tests were used. The $\chi 2$ test was used to compare categorical variables, and the Fisher Exact test was used when chi-square conditions could not be met.

RESULTS

During the study period, 48 of 456 patients with NI were included. The gender distribution was about equal. The median age of the patients was 32 months. Respiratory diseases (50%) such as pneumonia and asthma attacks were the most common reasons for admission to the PICU, followed by sepsis (22.9%) and trauma (12.5%). The median length of stay in the PICU was 25 days, ranging from 7 to 114 days, and 93.8% had hospitalizations longer than 7 days. The median PRISM III score was 8 (0-30). IMV was required in 41 patients (85.4%), and the median duration of IMV was 13 (3-102) days. Inotropic agents were used in 23 patients (47.9%). Fifteen patients (31.3%) underwent therapeutic plasma exchange (TPE), and 7 patients (14.6% of the total) had continuous renal replacement therapy (CRRT) (Table 1).

The most common pathogens identified were Gram-negative bacteria (33.3%) and fungus (27.1%) (Table 1). The rates of CRBSI, VAP, and CAUTI were 56.2%, 25%, and 18.7%, respectively (Table 2). The most frequent pathogens were *Pseudomonas aeruginosa*, *Klebsiella* species, and *Candida* species.

The mortality rate was 18.8%. According to the prognostic outcome in the PICU, patients were divided into the survival group (n=39) and the non-survival group (n=9). The requirement for CRRT was significantly higher in the non-survival group (p=0.017). Patients had similar prolonged PICU stay rates and requirements of IMV, TPE, and inotropic agents (p=0.472, p=0.320, p=0.432, p=0.068) (Table 3). PCT (p=0.015), and procalcitonin/albumin ratio (PAR) (p=0.016) were also higher in the non-survival group than those in the survival group (Table 4). Receiver operating characteristic

Table 1. Demographics, clinical characteristics of children with nosocomial infections

		n=48
Gender, n (%)	Male	27 (56.3%)
	Female	21 (43.8%)
Age (month), median (min-max)		32 (1.5-214)
PRISM III score		8 (0-30)
Etiologies of admission, n (%)	Respiratory diseases	24 (50%)
	Sepsis	11 (22.9%)
	Trauma	6 (12.5%)
	Neurological diseases	3 (6.3%)
	Other	4 (8.4%)
Mortality, n (%)		9 (18.8%)
Length of stay (day), median (min-max)		25 (7-114)
Length of stay >7 days, n (%)		45 (93.8%)
Requirement of IMV, n (%)		41 (85.4%)
Duration of IMV, days median (min-max)		13 (3-102)
Requirement of TPE, n (%)		15 (31.3%)
Requirement of CRRT, n (%)		7 (14.6%)
Requirement of inotropic agents, n (%)		23 (47.9%)
Pathogens, n (%)	Gram-positive bacteria	6 (12.5%)
	Gram-negative bacteria	16 (33.3%)
	Fungus	13 (27.1%)
	Multiple pathogens	12 (25.0%)

CRRT: Continuous renal replacement therapy, IMV: Invasive mechanical ventilation, PRISM III: Pediatric Risk of Mortality III, TPE: Therapeutic plasma exchange, min-max: Minimum-maximum

Table 2. Types of nosocomial infections

	n (%)
CRBSI	27 (56.2%)
VAP	12 (25%)
CAUTI	9 (18.7%)

CAUTI: Catheter-associated urinary tract infections, CRBSI: Catheter-related bloodstream infection, VAP: Ventilator-associated pneumonia

(ROC) curves were used to predict mortality with PCT and PAR. According to ROC analysis, the cut-off values for PCT and PAR were found to be 1.705 (p=0.015), and 0.538 (p=0.016) respectively (Table 5, Figure 1).

Table 3. Treatment modalities according to sepsis outcomes

	Outcome		p-value
	Mortality, n (%) (n=9)	Survival, n (%) (n=39)	
Length of stay >7 days	8 (17.8%)	39 (81.3%)	0.472
Requirement of IMV	9 (22.0%)	32 (78.0%)	0.32
Requirement of CRRT	4 (57.1%)	3 (42.9%)	**0.017**
Requirement of TPE	4 (26.7%)	11 (73.3%)	0.432
Requirement of inotropic agents	7 (30.4%)	16 (69.6%)	0.068

CRRT: Continuous renal replacement therapy, IMV: Invasive mechanical ventilation, TPE: Therapeutic plasma exchange

DISCUSSION

Children admitted to the PICU are particularly susceptible to NIs because of the high prevalence of the use of invasive devices during their hospitalization (10). NI is a significant cause of morbidity and mortality as well as a serious financial burden. The overall incidence of NI in our PICU was 10.5%, similar to the results reported in other studies. As in most pediatric studies, we found CRBSI to be the most frequent NI (11-13).

We found that Gram-negative bacteria and fungus were more common in NI. Several studies have found that Gram-negative bacteria are more frequently isolated than Gram-positive bacteria, despite conflicting findings regarding pathogens (14). The reason for the high incidence of fungal infections in this study may be the inclusion of atypical agents.

Table 4. Relationship between laboratory parameters and outcomes of sepsis patients

	Outcome		p-value
	Mortality, n (%) (n=9)	Survival, n (%) (n=39)	
Leukocyte	7850 (4660-23790)	10160 (50-34930)	0.061
Neutrophil	6160 (2700-21830)	7350 (0-32680)	0.342
Lymphocyte	1380 (810-2930)	1810 (0-7170)	0.240
Platelet	246000 (55000-327000)	242000 (7000-724000)	0.452
RDW	15.3 (14.7-18.3)	14.4 (11.4-20.0)	0.037
CRP	54.97 (0.6-229.23)	9.97 (0.04-386.11)	0.376
Procalcitonin	11 (0.23-334.24)	0.53 (0.03-315.52)	**0.015**
Lactate	1.27 (0.6-4.3)	1.5 (0.4-19.3)	0.711
LDH	489 (296-3340)	389 (173-2133)	0.178
Albumin	3.21 (1.97-3.98)	3.6 (1.2-4.73)	0.079
Lactate/albumin ratio	0.47 (0.15-1.63)	0.43 (0.1-5.24)	0.436
Neutrophil/lymphocyte ratio	4.10 (1.56-19.85)	2.93 (0.68-102.13)	0.516
CRP/albumin ratio	16.47 (0.15-96.32)	2.65 (0.01-153.05)	0.322
PCT/albumin ratio	3.23 (0.11-92.33)	0.171 (0.008-113.90)	**0.016**
LDH/albumin ratio	151.7 (77.8-1403.3)	106.4 (48.7-725.5)	0.11

CRP: C-reactive protein, LDH: Lactate dehydrogenase, PCT: Procalcitonin, RDW: Red cell distribution width

Table 5. Predictive characteristics of markers

	Cut-off threshold	Sensitivity (%)	Specificity (%)	AUC (95.0% CI)	p-value
Procalcitonin	1.705	77.8	66.7	0.764 (0.605-0.922)	0.015
PAR	0.538	77.8	64.1	0.761 (0.604-0.918)	0.016

AUC: Area under curve, PAR: Procalcitonin to albumin ratio, CI: Confidence interval

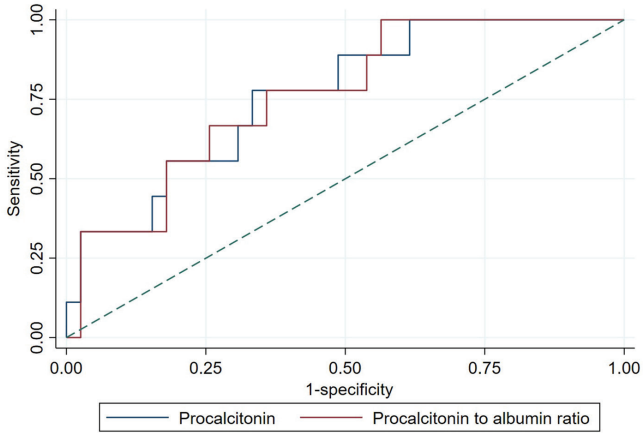

Figure 1. Analysis of ROC curves of mortality and biomarkers
ROC: Receiver operating characteristic

Most patients had prolonged stays in the PICU. This result was consistent with the literature and could be explained by the lengthier stay, more frequent invasive operations, and increased patient contact with medical staff (15,16). Furthermore, the adverse hemodynamic consequences of NI may worsen organ dysfunction in critically ill pediatric patients and escalate the requirement for supportive care (3).

Mortality of NI in our study was 18.8%, which is similar to that reported in developing countries and higher than that reported in developed counties. Mortality rates in developing countries ranged from 20% to 38%, whereas they were 7.7 % to 10% in developed countries (11,14,17-19).

Another remarkable aspect of our data is that there was no statistically significant difference when comparing non-survival and survival patients for other treatment modalities. The adverse hemodynamic consequences of NI may worsen organ dysfunction in critically ill pediatric patients and escalate the requirement for supportive care (3). There were not significant differences in terms of the length of PICU stay, requirement of TPE, or inotropic agents. However, non-survival patients had a greater requirement for CRRT. Presumably, in terms of the requirement of these treatment modalities, patients with NI should be fully compared with patients hospitalized in the PICU.

Along with cultures, conventional and widespread biomarkers, such as CRP and leukocyte count, are generally regarded as valuable for the diagnosis of infection (20). This particular approach is considered insufficient for early diagnosis because it may take between 24 and 72 h to obtain culture results. Given that delays in diagnosis may increase the risk of mortality, it is necessary to develop quicker and more effective diagnostic markers.

PCT demonstrated a high level of accuracy in predicting the presence of bacteremia in cases of infection. Consequently, it is advisable to use PCT in the assessment of bacterial infection and sepsis among critically ill patients because it has been found to potentially correlate with poor outcomes in patients (21-23). Moreover, albumin serves as a robust indicator of clinical disease outcomes because of its tendency to decrease during acute infections (24,25). There is a significant correlation between PCT and albumin. Therefore, the co-occurrence of PCT positivity and albumin negativity serves as a prognostic indicator in adult patients susceptible to bacterial infection. Some studies have suggested that PAR is a rapid and relatively inexpensive biomarker that can be used as an early marker to differentiate severe NIs (20,26). Consistent with the literature, we found that PCT levels and PAR of non-survival patients were significantly higher than those of survival patients.

The main limitations of this study were the small number of cases compared with studies in adults and the inclusion of only one tertiary center. The inclusion of multiplecenters could provide additional information and identify other prognostic factors in NIs among children. Second, the low positivity and lack of standardization in culture collection time may have affected the results of pathogen identification. Furthermore, our study did not describe all NIs, such as surgical incision infections.

CONCLUSION

NIs are an important preventable cause of increased morbidity and mortality in critically ill children. This prompts the question, as clinicians, of what we can do to reduce NIs. Risk factors should be considered in patients who cannot be changed, such as the underlying disease. Other modifiable risk factors for NIs will likely be the focus of efforts to enhance patient care.

ETHICS

Ethics Committee Approval: University of Health Sciences Türkiye, Sancaktepe Şehit Prof. Dr. İlhan Varank Training and Research Hospital Non-invasive Research Ethics Committee approval was received from the hospital (decision no: 29, date: 15.02.2023).

Informed Consent: We obtained informed consent from all parents before hospitalization and during all procedures.

Authorship Contributions

Concept: C.D., K.B.G., Design: K.B.G., Data Collection or Processing: E.G.Ş., Y.Y.C., Analysis or Interpretation: C.D., A.S., Literature Search: C.D., E.G.Ş., Y.Y.C., Writing: C.D., F.V.

Conflict of Interest: No conflict of interest was declared by the authors.

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